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# Two Novel Cocrystals of Lamotrigine with Isomeric Bipyridines and In Situ Monitoring of the Cocrystallization

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***Abstract***

Crystal engineering strategy was applied to develop new solid forms of lamotrigine. Two novel cocrystals of lamotrigine forming with 4,4′-bipyridine (2:1) and 2,2′- bipyridine cocrystal (1:1.5) were successfully obtained by neat grinding and liquid assisted grinding. The novel cocrystals were fully characterized and confirmed by X-ray diffraction, thermal and spectroscopic analysis. DXRxi Raman microscope was also used to identify the cocrystals. The factors such as solvent and the structure of coformers which influenced the cocrystal formation were discussed. Furthermore, the novel cocrystals were both obtained by slurry crystallization. Process analytical technologies including focused beam reflectance measurement and attenuated total reflectance fourier transform infrared were applied to investigate the cocrystallization process and the mechanism. HPLC analysis showed that the dissolution rate and the solubility of the two novel cocrystals were both improved.

**Key words**: lamotrigine; cocrystal screening; isomeric bipyridines; cocrystallization process; dissolution